Sub D3 C2 13. (Twice Amended) A method as in claim 4 wherein said at least one ligase is selected from the group consisting of Pfu DNA ligase, T4 DNA ligase, Taq DNA ligase, T4 RNA ligase, and E.coli DNA ligase.

Sub D8 29. (Twice Amended) A method as in claim 1 wherein said at least one nucleic acid polymerase is selected from the group consisting of Taq DNA polymerase, T4 DNA polymerase, Klenow fragment, Pfu DNA polymerase, Exo- Pfu DNA polymerase, E.coli DNA polymerase I, Klenow fragment of DNA polymerase I, MMLV reverse transcriptase and AMV reverse transcriptase. C3

Sub D9 33. (Twice Amended) A method as in claim 26 wherein said at least one ligase is selected from the group consisting of Pfu DNA ligase, T4 DNA ligase, Taq DNA ligase, T4 RNA ligase, and E. coli DNA ligase. C4

REMARKS

Reconsideration is requested.

Claims 1-40 are pending.

Claims 13 and 33 have been amended above to obviate the objection to claim 33 noted in paragraph 5 on page 4 of the Office Action dated February 28, 2001 (Paper No. 14). Withdrawal of the objection to claim 33 is requested.

The Section 112, second paragraph, rejection of claims 1-40 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Examiner indicates his belief that claims 1-40 are vague and indefinite as it is allegedly unclear how the total nucleic acid is measured via measuring the total

amount of the detectable species bound to a solid phase or measuring the total amount of at least one detectable species or binding species. One of ordinary skill in the art would appreciate, such as by reading the present specification at, for example, page 14, first full paragraph, that total nucleic acid may be measured by, for example, comparison to a standard curve generated using known amounts of DNA in the specific protocol.

Claims 8 and 29 have been amended to delete the reference to "(3'-5')" to obviate the Examiner's apparent confusion over the same.

Withdrawal of the Section 112, second paragraph, rejection of claims 1-40 is requested.

The Section 103 rejection of claims 1-3, 6-12, 14-25, 28-32 and 34-37 over Hartley (U.S. Patent No. 5,043,272) in view of Eberle (U.S. Patent No. 5,413,906) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The Examiner's detailed comments in response to the applicants' Remarks are appreciated. However the Examiner appears to have not viewed the present application and claims as a whole in comparison to the cited art. That is, a fundamental distinction between the presently claimed invention and the cited art is that the presently claimed invention provides a method of measuring total nucleic acid in a sample which has been amplified with at least one random primer. While providing elements of the presently claimed invention, the cited art does not teach or suggest the combination of these fundamental aspects of the presently claimed invention or motivation for one of

ordinary skill in the art to select these aspects of the art and combine them to make the presently claimed invention.

Specifically, Hartley describes in column 8, for example, that specific amplified sequences are identified or detected for applications in "medical diagnostics, agricultural, environmental and foodstuff monitoring, or any other use requiring the detection of specific DNA or RNA at low concentrations." See, column 8, lines 6-9 of Hartley (emphasis added). Moreover, Hartley describes the detection in identification of the presence of "pathogenic bacteria, yeast, protozoa, nematodes ... or viruses .... The nucleic acids present in the sample can be amplified to a point that probe sequences complimentary to characteristic sequences of the suspected pathogens can be used with a high degree of assurance for detection of their presence in the sample." See, column 8, lines 17-25 of Hartley (emphasis added). The applicants respectfully submit Hartley does not teach or suggest measuring total nucleic acid in a sample, as claimed. In fact, Hartley teaches away from the presently claimed method of measuring total nucleic acid in a sample by specifically teaching the use of specific probes for measuring and detecting specific sequences.

The Examiner has relied on Eberle at column 10, line 59 to column 11, line 9 (see, page 7 of Paper No. 14) in alleging that the disclosed method may be used for the detection of nucleic acid sequences. The Examiner will appreciate however that the method described at column 10, line 59 to column 11, line 9 of Eberle requires a specific promoter sequence, presumably as a template for amplification and subsequent detection. This promoter sequence template is not a mixed sample of sequences, as

may be used in the present invention. The presently claimed invention does not require such a specific template sequence as required by the method described in the passage relied upon by the Examiner in Eberle. There is no suggestion in Eberle that a mixed starting material could be used in place of the specific promoter sequence template described in the passage of Eberle noted by the Examiner.

Accordingly, the applicants respectfully submit that neither Hartley nor Eberle provide motivation to one of ordinary skill in the art to make the presently claimed invention. Moreover, Hartley teaches away from the present claimed method of measuring total nucleic acid in the sample and Eberle fails to cure the deficiencies in the primary reference. Withdrawal of the Section 103 rejection of claims 1-3, 6-12, 14-25, 28-32 and 34-37 over Hartley in view of Eberle is requested.

The Section 103 rejection of claims 4, 5, 13, 26, 27, 33 and 39-40 over Hartley in view of Wu (Genomics, 1989, vol. 4, pages 560-569) and Respess (U.S. Patent No. 5,599,662) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

As noted above, Hartley teaches away from the presently claimed invention providing a method which requires measurement of specific nucleic acid sequences rather than the presently claimed method of measuring total nucleic acid in the sample. The secondary references fail to overcome this deficiency of Hartley and further fail to provide any motivation for one of ordinary skill in the art to make the presently claimed invention. Accordingly, withdrawal of the Section 103 rejection of claims 4, 5, 13, 26, 27, 33 and 39-40 over Hartley in view of Wu and Respess is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is invited to contact the undersigned if anything further is required in this regard.

Respectfully submitted,

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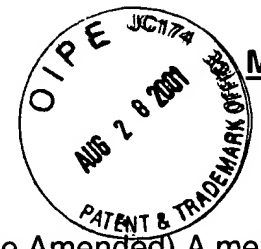

MARKED UP CLAIMS

8. (Twice Amended) A method as in claim 1 wherein said at least one nucleic acid polymerase is selected from the group consisting of Taq DNA polymerase, T4 DNA polymerase, Klenow fragment [(3'-5')], Pfu DNA polymerase, Exo- Pfu DNA polymerase, E.coli DNA polymerase I, Klenow fragment of DNA polymerase I, MMLV reverse transcriptase and AMV reverse transcriptase.

13. (Twice Amended) A method as in claim 4 wherein said at least one ligase is selected from [then] the group consisting of Pfu DNA ligase, T4 DNA ligase, Taq DNA ligase, T4 RNA ligase, and E.coli DNA ligase.

29. (Twice Amended) A method as in claim 23 wherein said at least one nucleic acid polymerase is selected from the group consisting of Taq DNA polymerase, T4 DNA polymerase, Klenow fragment [(3'-5')], Pfu DNA polymerase, Exo- Pfu DNA polymerase, E.coli DNA polymerase I, Klenow fragment of DNA polymerase I, MMLV reverse transcriptase and AMV reverse transcriptase.

33. (Twice Amended) A method as in claim 26 wherein said at least one ligase is selected from [then] the group consisting of Pfu DNA ligase, T4 DNA ligase, Taq DNA ligase, T4 RNA ligase, and E. coli DNA ligase.